



# U.S. Scientific Update

## Aricept 23 mg Tablets

**Dr. Lynn Kramer**  
**President**  
**NeuroScience Product Creation Unit**  
**Eisai Inc.**

*hvc*  
*human health care*

# Unmet Need in Moderate to Severe Alzheimer's Disease (AD)



- **Ongoing clinical deterioration associated with further loss of cholinergic neurons**
- **Current treatment options include acetylcholinesterase inhibitors + memantine**
- **Will moderate to severe Alzheimer's Disease patients benefit from higher doses of acetylcholinesterase inhibitors?**
- **First study to evaluate efficacy and safety of higher-dose donepezil (23 mg/day vs 10 mg/day) in this patient group**

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# Effectiveness and Tolerability of High-Dose (23 mg/day) Versus Standard-Dose (10 mg/day) Donepezil in Moderate to Severe Alzheimer's Disease: A 24-Week, Randomized, Double-Blind Study

**Farlow MR, Salloway SP, Tariot PN, Yardley J, Moline M, Wang Q,  
Zou H, Brand-Schieber E, Hsu T, Satlin A**

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# Summary View

## High-Dose Hypothesis Proven



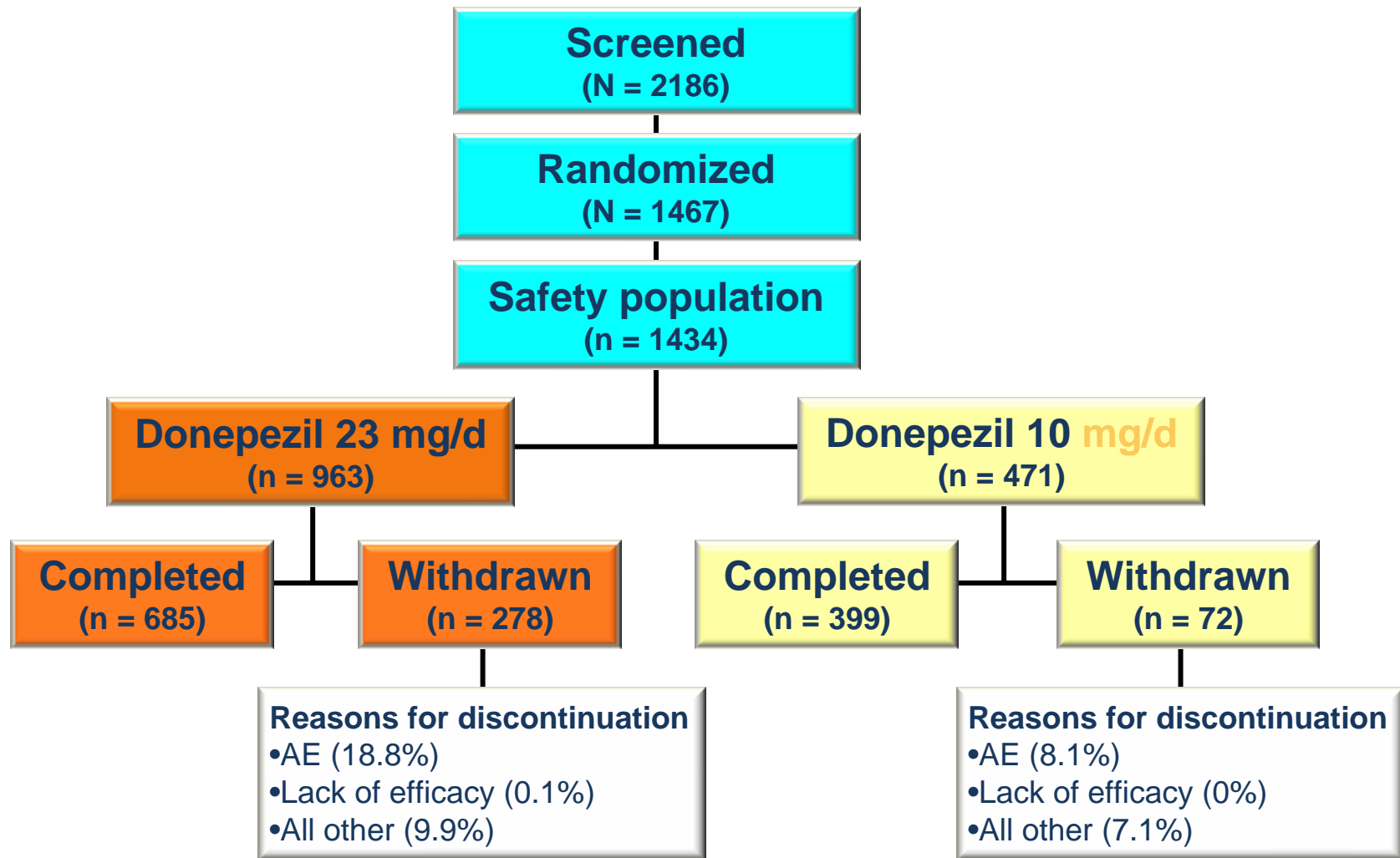
- Study 326 basis of U.S. Food and Drug Administration approval of Aricept 23 mg tablets
- Aricept 23 mg/day demonstrated additional benefit over 10 mg tablet in patients with moderate-to-severe Alzheimer's Disease
  - Robust cognitive results as measured by the Severe Impairment Battery (SIB)
- Addresses unmet medical need
  - Aricept 23 mg tablets may provide benefit to moderate-to-severe Alzheimer's Disease patients
- Aricept may not be for everyone. Please see the full Important Safety Information and Prescribing Information at the end of this presentation.

# Study Overview



- **Design**
  - **24-week, double-blind comparison of donepezil 23 mg/day with donepezil 10 mg/day**
  - **Study powered for superiority**
  - **Randomization 23 mg/day:10 mg/day, 2:1**
  - **Co-primary endpoints: Severe Impairment Battery (SIB), Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC+)**
  - **Safety**
- **Population**
  - **Moderate-to-severe AD (Mini-Mental State Examination (MMSE 0-20))**
  - **On Aricept 10 mg IR for a minimum of 3 months before Screening**
  - **Patients taking memantine for at least 3 months before Screening could be enrolled**
  - **N=1467**

# Patient Disposition

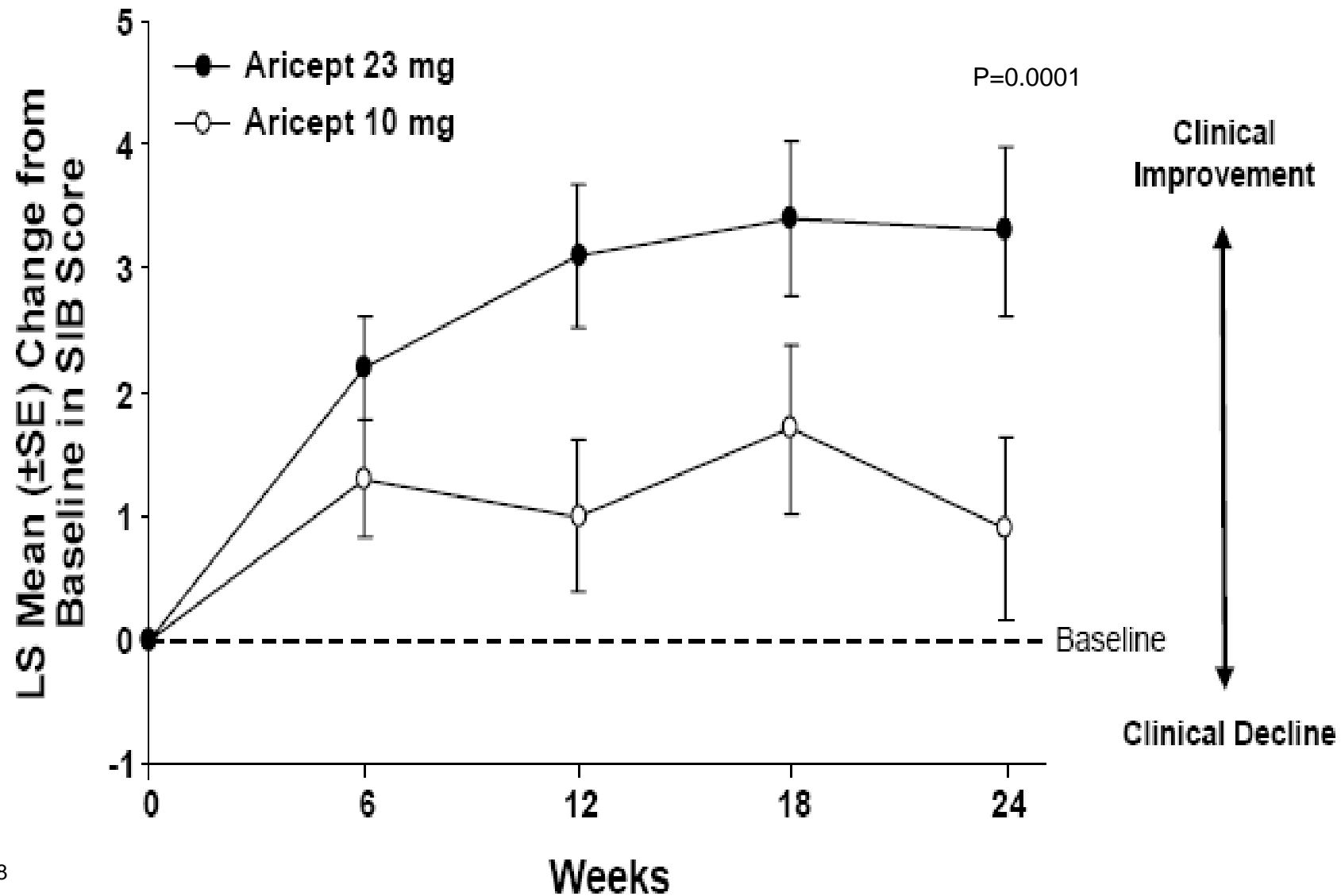


# Demographics Similar Between Groups



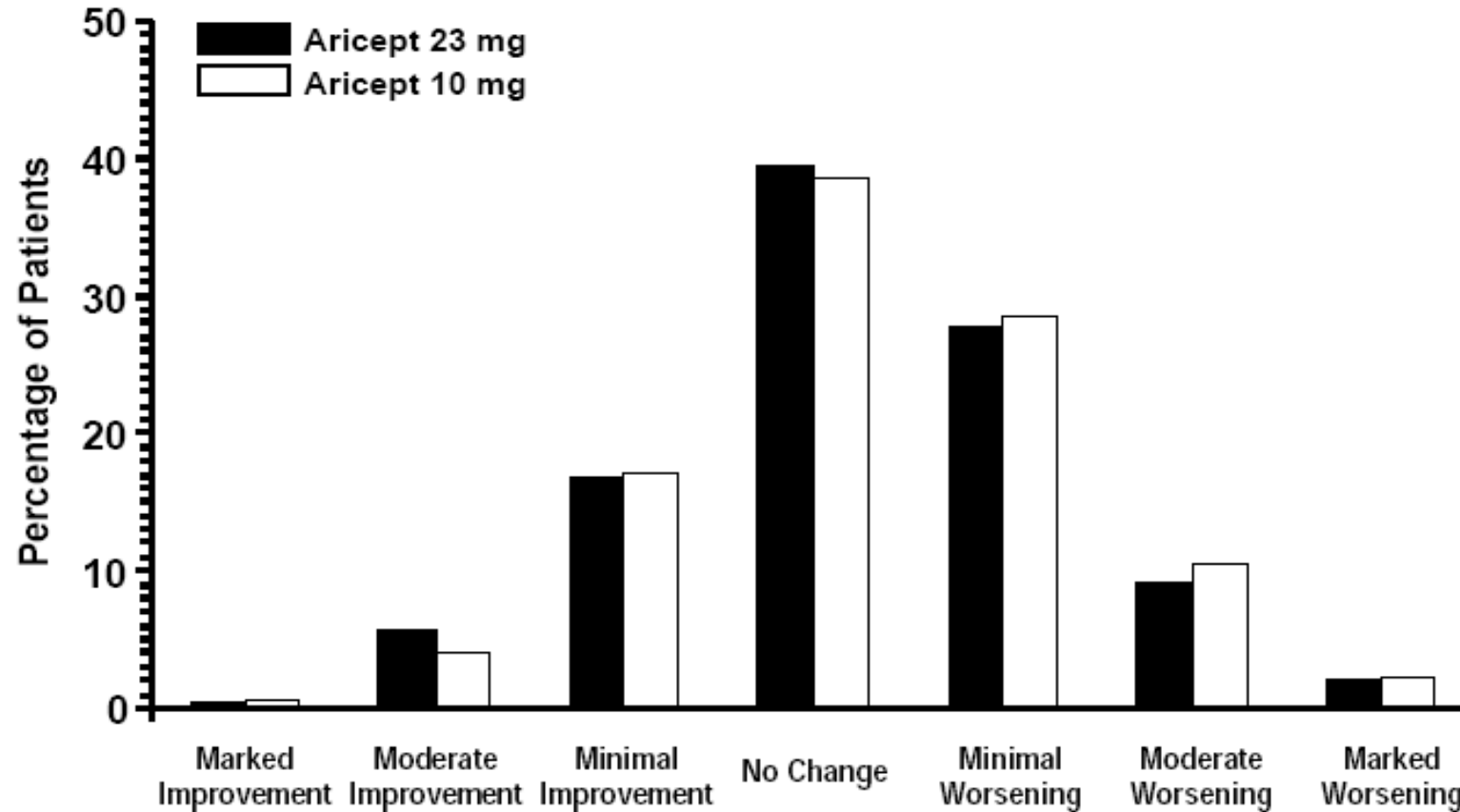
	Donepezil 23 mg/day	Donepezil 10 mg/day
Safety population	963	471
<b>Mean age (SD)</b>	<b>73.9 (8.5)</b>	<b>73.8 (8.6)</b>
<b>Females (%)</b>	<b>63.0</b>	<b>62.4</b>
<b>Type of residence (%)</b>		
Lives alone	3.5	6.4
Lives with caregiver, relative, or friend	91.1	87.1
Senior residence, retirement home, assisted living facility	3.6	5.3
Other	1.8	1.2
<b>Duration (weeks) of donepezil 10 mg/day use prior to study, mean (SD)</b>	<b>112 (108)</b>	<b>105 (99)</b>
<b>Concomitant memantine at baseline (%)</b>	<b>36.6</b>	<b>35.7</b>

# SIB: Change from Baseline (ITT Population)





# CIBIC+: Overall Change Score at Week 24 (ITT Population)



*The mean difference between the 23 mg/day and 10 mg/day treatment groups was 0.06 units. This difference was not statistically significant.*

# Most Frequent Adverse Events Leading to Discontinuation, by Treatment Group



<b>Dose Group</b>	<b>23 mg/day Aricept</b>	<b>10 mg/day Aricept</b>
<b>Safety Population</b>	<b>963</b>	<b>471</b>
<b>Event/% Discontinuing</b>		
<b>Vomiting</b>	<b>3</b>	<b>0</b>
<b>Diarrhea</b>	<b>2</b>	<b>0</b>
<b>Nausea</b>	<b>2</b>	<b>0</b>
<b>Dizziness</b>	<b>1</b>	<b>0</b>

# Most Common AEs

Occurring in  $\geq 2\%$  of Patients in Donepezil 23 mg/day Group and With Higher Frequency Than Donepezil 10 mg/day Group



Preferred Term (% of subjects)	Donepezil 23 mg/d	Donepezil 10 mg/d
Safety population	963	471
% of patients with at least 1 AE	74	64
Nausea	12	3
Vomiting	9	3
Diarrhea	8	5
Anorexia	5	2
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Dizziness	5	3
Weight decreased	5	3
Headache	4	3
Insomnia	3	2
Urinary incontinence	3	1
Fatigue	2	1
Asthenia	2	1
Contusion	2	0
Somnolence	2	1

# New FDA Approved Labeling

## Aricept 23 mg tablets



- **Dosage and Administration**
  - Mild to Moderate Alzheimer's Disease – 5 mg or 10 mg administered once daily
  - Moderate to Severe Alzheimer's Disease – 10 mg or 23 mg administered once daily
- **A dose of 10 mg once daily can be administered once patients have been on a daily dose of 5 mg for 4 to 6 weeks.**
- **A dose of 23 mg once daily can be administered once patients have been on a dose of 10 mg once daily for at least 3 months.**

# Potentially Important Pharmacokinetic Differences



- Both tablets administered once daily
  - Consistent with half-life >70 hours
- PK of Aricept 23 mg/day versus Aricept 10 mg/day (population PK from Study 326)
  - Peak plasma concentration is achieved for Aricept 23 mg tablets in approximately 8 hours, compared with 3 hours for Aricept 10 mg tablets.
  - Peak plasma concentrations were almost 2-fold higher for Aricept 23 mg tablets than Aricept 10 mg tablets
- The 23 mg tablet should not be crushed or chewed because this may increase its rate of absorption

# Summary



- The study showed that patients on 23 mg/day experienced important clinical benefit on both measures compared to 10mg/day
  - Increasing the donepezil daily dose to 23 mg/day provided statistically significant cognitive benefit (SIB) compared to continuing 10 mg/day in patients with moderate to severe AD
  - Donepezil 23 mg/day did not provide statistically significant incremental benefit compared to 10 mg/day on global function (CIBIC+) in the overall ITT population
- In the pivotal study there were no important differences in the type of adverse events in patients taking donepezil with or without memantine
- The most frequent adverse events for Aricept 23 mg/day were nausea, vomiting, diarrhea and anorexia
- Aricept may not be for everyone. Please see the full Important Safety Information and Prescribing Information at the end of this presentation.

# Important Safety Information



**Aricept may not be for everyone. People at risk for stomach ulcers or who take certain other medicines should tell their doctors because serious stomach problems, such as bleeding, may get worse.**

**People at risk for certain heart conditions should tell their doctor before starting Aricept because they may experience fainting. People with serious lung conditions and difficulty breathing, bladder problems or seizures should tell their doctor before using Aricept. Aricept 23 mg/day is associated with weight loss. Check with the doctor if this is a concern. Inform the doctor if the patient needs surgery requiring anesthesia while taking ARICEPT.**

**Some people may have nausea, diarrhea, difficulty sleeping, vomiting or muscle cramps. Incidence of nausea and vomiting were markedly greater in patients taking Aricept 23 mg/day versus patients taking Aricept 10 mg/day. Some people may feel tired or may have loss of appetite. If they persist, please talk to the doctor.**

**For Full Prescribing and Patient Information, please visit [www.aricept.com](http://www.aricept.com).**

# Safe Harbor Statement



- **Materials and information provided during this presentation may contain so-called “forward-looking statements.” These statements are based on current expectations, forecasts and assumptions that are subject to risks and uncertainties which could cause actual outcomes and results to differ materially from these statements.**
- **Risks and uncertainties include general industry and market conditions, and general domestic and international economic conditions such as interest rate and currency exchange fluctuations. Risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, technological advances and patents attained by competitors; challenges inherent in new product development, including completion of clinical trials; claims and concerns about product safety and efficacy; obtaining regulatory approvals; domestic and foreign healthcare reforms; trends toward managed care and healthcare cost containment; and governmental laws and regulations affecting domestic and foreign operations.**
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- **The Company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.**





# U.S. Commercial Launch Plan

## Aricept 23 mg Tablets

**Mr. Lonnel Coats**  
**President and CEO**  
**Eisai Inc.**

*hvc*  
human health care

# Important Updates – Aricept 23 mg Tablets



- FDA approval has occurred for U.S. market
- Eisai / Pfizer commercial organizations prepared and ready to launch with 1300 medical representatives in U.S.
- Eisai national launch meeting to occur within 9 days post FDA approval, via national web-cast to 46 sites across U.S.
- Pfizer plans launch within the week for their field force
- Product availability in pharmacies within 9 days post FDA approval
- Aricept 23 mg tablets launch in U.S. market will provide a new dosing option to moderate-to-severe AD patients who may benefit from this new product

# Aricept 23 mg Tablets May Address Unmet Needs in the Market



- Caregivers of moderate-to-severe Alzheimer's Disease patients are continually searching for additional therapeutic options
- Aricept 23 mg tablets may provide greater cognitive efficacy for moderate-to-severe Alzheimer's Disease as compared to Aricept 10 mg tablets
- Aricept may not be for everyone. Please see the full Important Safety Information and Prescribing Information at the end of this presentation

# Opportunity at Launch



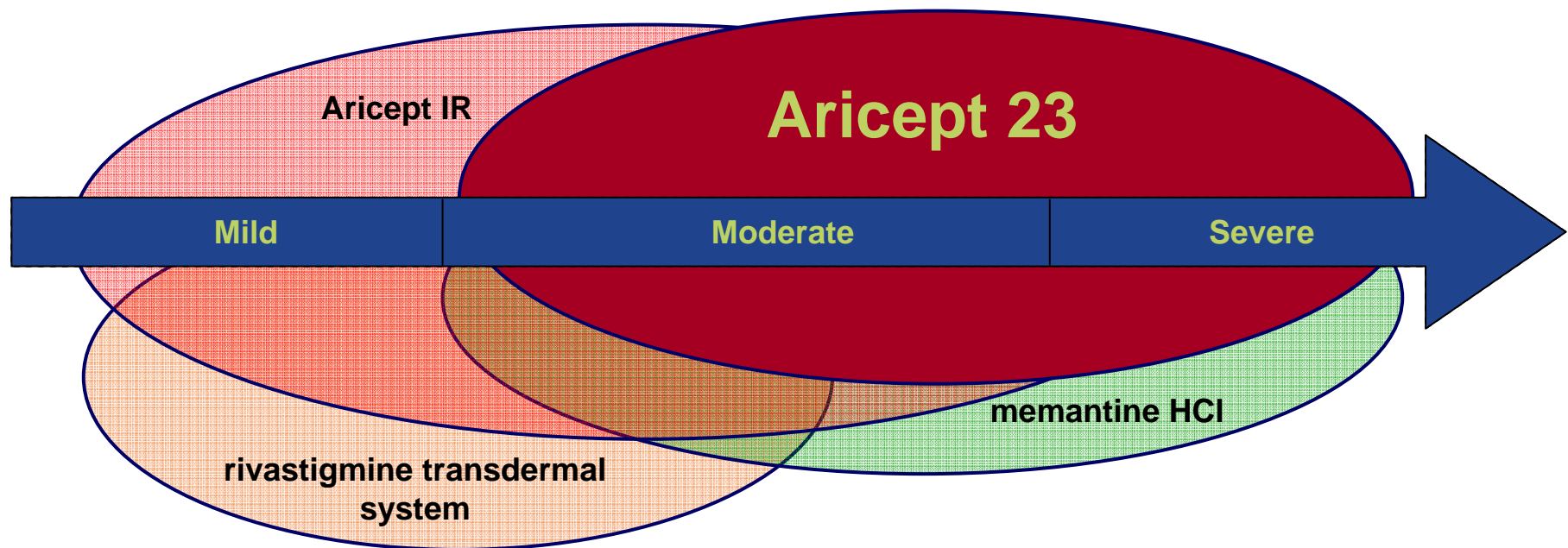
- 63% of all AD patients are currently on Aricept 5 mg or 10 mg tablets
- Over 75% of Aricept patients are currently on the 10 mg dose
- Approximately 70% of patients on Aricept 10 mg/day are moderate-to-severe and may gain additional benefit by increasing to once-daily 23 mg tablets
- Target peak U.S. sales: \$600M+ by 2012
- Aricept may not be for everyone. Please see the full Important Safety Information and Prescribing Information at the end of this presentation

Data Sources: IMS NPA, IMS Retail Patient Tracker

# Opportunity for Aricept 23 mg Tablets to Capture Moderate-to-Severe Segment



- **Focus opportunity in moderate segment - 45% of all AD patients**
  - in line with indication, largest patient segment



# Recent Eisai Activities at International Congress on Alzheimer's Disease (ICAD)



- **Eisai had significant presence at ICAD conference (July 2010)**
- **For Aricept 23 mg tablets:**
  - Oral presentation of pivotal study, “Effectiveness and Tolerability of High Dose (23mg/d) Versus Standard-Dose (10mg/d) Donepezil in Moderate-to-Severe Alzheimer’s Disease,” by Dr. Martin Farlow, Professor & Vice-Chairman of Research in Department of Neurology, Indiana University
  - Poster: Safety profile of higher dose
  - Poster: Patients with more advanced Alzheimer’s Disease

# Aricept 23 mg Tablet Managed Care Contract Strategy



- **Opportunity:**
  - Focus on key accounts in both Medicare Part D and Commercial Business that make up ~ 90% of Aricept 23 mg tablet opportunity
- **Objective:**
  - Secure and/or protect Aricept 23 mg tablet Tier 2 formulary positioning
- **Strategy:**
  - Leverage existing Aricept contracts to maintain Aricept 23 mg tablet formulary access
- **Pricing:**
  - Maintain parity pricing to the current 5 mg and 10 mg tablet

# Summary



- New market opportunity created for patients who would have to choose no therapy or expensive combination therapy
- Study results showed that patients on 23 mg/day experienced important clinical benefit on both measures compared to 10 mg/day
  - Severe Impairment Battery (SIB) -  $p=0.0001$  (statistically significant)
  - Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC+) –  $p=0.1789$  (not statistically significant)
- Excellent managed care strategy in place to provide optimal access for patients
- Eisai and Pfizer are excited and aligned to launch Aricept 23 mg tablets within U.S. market 9 days post FDA approval with 1300 MRS
- Parity pricing to encourage patients to start and stay with Aricept as their disease progresses
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